III. REMARKS

Claim Status

Claims 1-2 and 5-13 are under current examination. Claims 1-2 and 10-13 stand rejected; claims 5-9 stand objected to. In the advisory action the examiner did not enter applicant's amendment after final because it did not place the application in condition for allowance. In a subsequent telephonic interview graciously consented to by the examiner, the examiner confirmed that in her view a functionality limitation introduced in connection to the homology limitation would not be sufficient absent additional structural information to overcome the 35 USC 112 paragraph 1 rejection.

Claim Objections

Claims 5-8 are objected to because the claims contain the word, "SEQ ID" which the examiner suggests should be rewritten as "SEQ ID NO:"

This informality has been corrected in the amended claims. In the advisory action the examiner agreed that this amendment would overcome this ground for rejection.

Claim Rejections - 35 USC § 112

Claims 1-2, and 10-13 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because while claim 1 is broadly drawn, such that it applies to any a genus of Gaq-Gustducin chimeric G-

protein wherein the last 44 amino acids of the Gaq protein sequence are replaced with a 44 amino acid unit of Gustducin, the working examples provided in the instant application only demonstrate individual species of Gaq-Gustducin chimeric G-protein, specifically SEQ ID NO:2.

The examiner states that although the specification has support for the claim language of the newly amended claim 1, the specification does not define which 44 amino acids of Gustducin can be used to replace the C-terminus of the G protein.

Considering the potentially large numbers of polypeptides encompassed by these claims, the examiner states that the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention (genus) commensurate to its scope at the time the application was filed.

Applicant traverses this ground for rejection and although applicant has amended certain of the claims to permit early allowance of those more limited claims, applicant believes the more broadly stated claims are also supported by the disclosure of the specification.

1. Specifically Identified Chimera

The examiner has previously indicated that claims 5 to 9 are allowable but objected to as being dependent upon a rejected claim. Applicant has amended claim 1 to include the limitation of claim 5 and cancelled claim 5. Thus, all of claims 1-2 and 6-13 should now be allowable.

2. Homology at the C-terminus 44 amino acid unit

Applicants newly presented claims 18-20 and 27-34 read on a chimeric protein in which 44 amino acids the C-terminus of the G protein are replaced by a homologue of Gustducin of varying homology to SEQ ID NO.:2 where the homologues differ in the introduced 44 amino acid C-terminus, thus structurally defining the chimeric protein and meeting the examiners objection to the previously presented claims.

Basis for this limitation appears in paragraphs [0007], [0014], and [0019] of the published application.

Paragraph [0007] describes the current art belief, as set forth in paragraph [0006], that umami and bitter taste receptors couple to $G_{\alpha i}$ type G proteins such as Gustducin but are not be expected to efficiently couple to a $G_{\alpha q}$ type G protein such as $G_{\alpha 16}$.

As set forth in paragraph [0009] the substitution of the last at least 5 amino acid units at the C terminus of a $G_{\alpha q}$ type G protein with those of Transducin is known to the art but the coupling efficiency of that chimeric protein on human bitter, sweet or umami taste receptors is unknown.

Paragraph [0014] discloses an embodiment where at least the last 5 amino acids, preferably the last 44, amino acids of a $G_{\alpha q}$ type G protein are replaced with those of Gustducin.

Paragraph [0019] indicates that in specific embodiments 80%, 90% and most preferably 95% homologues of the chimeric proteins of paragraph [0014] may be utilized.

Thus, newly presented claims 18-20 and 27-34 are in accordance with the examiners request for further structural identification and should now be allowable.

3. Homology at other portions of the chimeric protein

Newly presented claims 18-20 claim homologues of the chimeric protein of claim 1 where the differences in structure may appear throughout the amino acid sequence. The examiner has rejected applicants claims claiming an 80% homology.

The amino acid sequence of SEQ ID NO.:2 is 1122 units long. At 80% homology, 224 amino acids may be modified; at 90%, 112; at 95%, 56. The chimera of the present invention show enhanced coupling with three distinct taste receptors. A modification at various positions in the sequence may minimize the effectiveness of the chimera to couple to one of the taste receptors but it is unlikely to so degrade its functionality with regard to all three that it is no longer useful for its intended purpose.

Support for homologues where the homologous species vary in portions of the molecule other than the C-terminus end appears in paragraphs [0018] and [0019] where varying levels of homology are specified and supported.

4. Homology plus functionality

Newly presented claims 24-27 claim homologues of the chimeric protein of claim 1 where the differences in structure may appear throughout the amino acid sequence and where the chimera are limited to those homologues where “the chimeric protein binds to one or more of the human bitter, sweet and

umami taste receptors." This expressed function limitation narrows the claimed invention to those chimera that are functional in their intended use and which can be easily determined by the procedures set forth in applicants specification therefore not requiring such undue experimentation as would make the claim indefinite.

Applicant believes the amended claims fully meet the requirements of the statute and are therefore are in form for allowance, which is respectfully requested.

However, the examiner has maintained the rejection of claims because of the presence of the phrase "wherein the resulting Gaq-gus44 chimeric G-protein has a sequence homology of at least 90% to SEQ ID NO:2".

Applicant traverses this continuing partial rejection.

As a first response, applicant would point out that in the last three months alone, the patent office has issued at least 8 patents containing claims directed to sequences having 90% homology to a specified sequence [USP 7,326,553; 7,312,058; 7,300,786; 7,297,759; 7,297,521; 7,316,914; 7,312,325; 7,294,499; 7,297,528; 7,291,454] where the sequence may be a nucleotide sequence or an amino acid sequence.

The examiner has stated that the applicant has not described the "structurally important features" of the genus of proteins which are at least 90% homologous to SEQ ID NO:2.

Insistence on the description of "structurally important features" beyond the degree of homology appears to be inconsistent with patent office practice as indicated above. The

purpose of the presence in the claim of a required degree of homology to a known sequence is the "structurally important feature" and identifies the genus. Here the claims are directed to sequences having 80%, 09% or 95% homology to SEQ ID NO.:2.

The other feature described in certain of the newly presented claims is that the homologue must bind to a receptor selected from bitter taste receptors, sweet taste receptors and umami taste receptors.

For these reasons applicant believes the claims are properly supported by the disclosure of the specification and respectfully request favorable reconsideration.

Claim Rejections - 35 USC § 103

Claims 1-2, and 10-13 are rejected under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873).

The previous office action rejected Claims 1-6 and 9-17 under 35 U.S.C. 103(a) as being obvious over Margolskee (USP 5,817,759) in view of Yao et al. (USP 7,041,457).

Applicant's response to the previous office action overcame this rejection which was expressly withdrawn. Applicant, in the unentered amendment, limited his argument to the newly cited reference since the rejection over the first two references had already persuaded the examiner.

The examiner, in the Advisory Action, states that the

applicant argues the references individually. Applicant respectfully disagrees. The first two cited references have already been overcome on the record.

Thus, the only additional art is Ruiz-Avila et al. The examiner utilizes Ruiz et al., at pages 8, 10 and 11 of the Office Action, as art teaching that the interaction of Gustducin with its cognate taste receptors is similar to that of transducing with rhodopsin. Ruiz-Avila et al. is also used as art disclosing the nexus between Gustducin and transducing homology and the importance of the C-terminus for interacting with taste receptors.

In applicant's response to the last office action applicant highlighted the fact that page 4 of the specification states:

> "Surprisingly we have now found that chimeric G-proteins based on Gaq-Gustducin are able to bind to a wide range of known and putative bitter taste receptors, and sweet and umami receptors with high affinity.

and that Margolskee does not disclose chimeric proteins.

Ruiz-Avila et al. is cited by the examiner as disclosing the importance of the C-terminus for interacting with taste receptors. But this is already disclosed by Yao et al. In Yao et al.'s claim 1 the claim requires the replacement of at least 5 amino acid residues from the C-terminus of a mutated Gq protein. Yao et al. state, in their specification:

> For instance, the present inventors have also discovered that the Gly to Asp mutation is synergistic

> with the replacement of the C-terminus of $G\alpha_q$ by that of transducin or $G\alpha_{olf}$. $G\alpha_q$ proteins containing C-terminal amino acids from transducin or $G\alpha_{olf}$ in combination with a Gly66 to Asp alteration show increased activity compared to individual chimeras alone. A preferred embodiment is a variant G_q proteins having at least about five amino acids in the C terminus of said G_q protein replaced by at least about five amino acids from the C terminus of $G\alpha_{olf}$, if or transducin, wherein said C-terminal substitution increases promiscuity of said variant G_q protein as compared to the corresponding native G_q protein. Up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated. Other possible variants are shown in FIGS. 3 and 4.

Thus, the disclosure of Yao et al. already shows the importance of C-terminal amino acids and this aspect of Ruiz-Avila et al. is merely additive to Yao et al. The examiner, having already acknowledged that applicants have overcome the Yao et al. in the previous action, has not made out a new *prima facie* case or added any new disclosure.

Yao et al. is directed to chimeric proteins and discloses a Gaq-transducin44 chimeric protein that is 58% homologous to the G16gust44 chimeric protein of the invention i.e. very much different from the claimed chimeric G-Proteins which are 90% homologous to SEQ ID NO:2.

Margolskee merely discloses Gustducin, but no chimeric G-

proteins. Ruiz-Avila et al. is also not directed to chimeric G-proteins either, and does not disclose the suitability or interchangeability of either transducin or gustducin in a chimeric G-protein.

Ruiz-Avila et al. exclusively addresses the natural interaction of gustducin and, commenting on various studies, mentions that the latter suggest that the interaction of gustducin with its cognate taste receptors, a key determinant of which is its C-terminus, may be similar to that of transducin with rhodopsin. Notably, the latter does not suggest anything in terms of actual functionality of one or the other partial protein in a chimeric protein, neither correct folding, coupling efficiency of the G-protein to the chimeric receptor nor resulting signal strength. This is significant in light of the fact that the **native** versions of the claimed G-proteins (G15, G16 and their homologs) do not couple effectively, in contrast to the **chimeric** G-proteins that are claimed.

Therefore, the addition of Ruiz-Avila as a third document does not disclose information that would allow one skilled in the art to arrive at the invention - the skilled person finds no direction whatsoever on which components may be combined in which way to result in a fully functional chimeric G-protein, much less a chimeric G-Protein with an improved coupling efficiency.

An artisan would therefore not be motivated to make the claimed chimeric G-Protein, nor would have expected success based on Yao et al.'s chimeric G-Proteins, which share only

about 60% homology with the claimed chimeric Gaq-gust44-Proteins.

Applicants believe the amendments to the claims and the above explanations are sufficient to negate any *prima facie* case of obviousness and respectfully request favorable reconsideration and allowance of these claims.

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

Respectfully submitted,
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